
PHARMACEUTICAL SCIENCES

**REVISION OF EXHIBIT BATCH REQUIREMENTS FOR
ABBREVIATED ANTIBIOTIC APPLICATIONS (AADA's)**

CONTENTS**PURPOSE****BACKGROUND****POLICY AND PROCEDURE****EFFECTIVE DATE**

PURPOSE

- To revise the requirements for Abbreviated Antibiotic Drug Applications (AADA's) with respect to the number and size of exhibit batches manufactured to support the filing of an original application.
-

BACKGROUND

- In 1945, Congress enacted section 507 of the Food, Drug, and Cosmetic Act establishing FDA's authority to regulate antibiotic drug products. At that time, all antibiotics were produced by fermentation. The fermentation, extraction and purification techniques then in use did not provide a high level of assurance that successive batches of a product of standard quality could be obtained. Therefore, the statute required that FDA conduct batch testing and certify the quality of individual batches of antibiotics post-approval. In its implementing regulations, the FDA required that acceptable performance data from three exhibit batches be submitted in support of an application.
 - After the statute was enacted, fermentation and purification technology gradually improved, and production of semi-synthetic and synthetic antibiotic drugs was introduced. Although these technological advances have improved the consistency of the manufacturing processes and the purity of antibiotic drug substances, fermentation processes continue to have some inherent variability.
 - In 1982, after many years of experience with the certification process, the FDA determined that the manufacturers of antibiotic drugs were demonstrating a high level of consistency in the quality of their products and exempted antibiotics from individual batch testing and certification requirements.
 - Shortly after the requirement for individual batch certification was eliminated, the FDA began to require that AADA applicants manufacture finished product exhibit batches that were at least 15-20% of the
-

proposed production batch size. This requirement was imposed because FDA believed this size exhibit batch would provide data that would be representative of full production-sized batches.

- Different requirements were developed for non-antibiotic drug products marketed under approved abbreviated new drug applications (ANDA's) because these drug products were regulated by a different organizational component within the FDA, and the requirements evolved differently. For ANDA products, FDA required preparation of one batch of at least 10% of the proposed commercial batch size. For solid, oral dosage forms, the requirement was one batch of at least 10% of the proposed commercial batch size or 100,000 dosage units, whichever was greater.
 - The Office of Generic Drugs (OGD), which now has responsibility for reviews of both ANDA's and AADA's, has concluded that a more consistent approach should be adopted for ANDA's and AADA's, although complete consistency is not possible because of the variability still inherent in the fermentation process.
-

POLICY AND PROCEDURE

- **Drug Substance**
 1. For AADA bulk antibiotic drug substances produced by fermentation, stability data must be provided on three production-scale batches, at least two of which should be generated from different starter cultures.
 2. For AADA bulk drug substances produced by semi-synthetic or full chemical synthesis, stability data must be generated on at least one batch which is at least 10% of the proposed commercial batch size. The batches should be prepared under conditions which meet the provisions of CDER MAPP 5223.3.
 - **Drug Product**
 1. For AADA drug products, other than solid, oral dosage forms, primary stability data (and bioequivalence data, if required) must be generated for each drug product on one batch that is at least 10% of the proposed commercial batch size and prepared under conditions which meet the provisions of CDER MAPP 5223.3.
 2. For solid, oral dosage form antibiotics, primary stability data (and bioequivalence data, if required) must be generated from one batch that is at least 10% of the proposed commercial batch size or 100,000 finished dosage units, whichever is greater. The exhibit batch must be prepared under conditions which meet the provisions of CDER MAPP 5223.3.
-

EFFECTIVE DATE

This guide is effective upon date of publication.